REMARKS/ARGUMENTS

Regarding the recent Advisory Action, Applicants apologise for the oversight in submitting the previous claim amendments on December 17, 2009 without fully removing the phrase "mRNA transcribed therefrom or protein encoded thereby" from the claims. The complete strikeout format was inadvertently lost during copy/paste. The claim amendments are resubmitted with all the references to the phrase removed. The previous remarks from the December 17, 2009 response are found below.

Applicants thank Examiner Dunston for the telephonic interview held on December 3, 2009, in which amendments to the claims were discussed. In light of the EST (SEQ ID NO:36) identified in the claims, the Examiner and Applicants' attorney agreed that removal of the language "mRNA transcribed therefrom or protein encoded thereby" in conjunction with the remarks submitted herewith regarding primer/probe design would be sufficient to overcome the outstanding enablement and written description-based rejections. Accordingly, the claims have been amended to reflect this agreement, and dependent claims referring to mRNA and/or protein detection have been cancelled. As the amendments to the claims do not recite new subject matter, Applicants submit that no new search is required, and respectfully request entrance of these after final amendments.

Applicants have amended the specification to capitalize the trademarks advertently missed in the previous amendment to the specification.

Rejection Under 35 U.S.C. §112, First Paragraph

Enablement Rejection

The Office has rejected the previously pending claims as allegedly lacking enablement due to recitation of "SEQ ID NO: 36". Specifically, the Office alleges that, because W26469 (SEQ ID NO:36) is an EST, there is insufficient information to identify the level of mRNA transcribed from or protein encoded by SEQ ID NO:36. The mRNA and protein language has been removed from the pending claims, rendering this aspect of the enablement-based

rejection moot. However, the Office also expresses concern regarding detecting the level of expression of SEQ ID NO:36 because the probe sequences on the Affymetrix array that Applicants used to detect differences in expression of SEQ ID NO:36 are not disclosed in the specification. In particular, the Office contends that detection of SEQ ID NO:36 with, e.g., Northern blot, reverse transcription PCR, or real time quantitative PCR could be difficult absent such probe information because "[i]f oligonucleotide probes were made from the sequence of SEQ ID NO:36, those probes are likely to hybridize to different genes located on different human chromosomes (see ht BLAST result in Appendix I, mailed 6/19/2009)." As a result, the Office concludes that undue experimentation would be required to detect the level of expression of SEQ ID NO:36. For the following reasons, that rejection is respectfully traversed.

First, Applicants actually detected the level of W26469 (SEQ ID NO:36) using Affymetrix microarray technology with RNA extracted from renal biopsies. The particular Affymetrix chip used to detect the level of W26469 was HG-U95av2 microarray -- which is a commercially available array. Moreover, the 16 different W26469 probes present on the HG-U95av2 microarray are publicly known – as Affymetrix provides such probe information online at:

https://www.affymetrix.com/products_services/arrays/specific/hgu95.affx#1_4

The W26469 probes present on the HG-U95av2 microarray are identified in Table 1 of the specification as belonging to probe set 31377_r_at. One can easily determine from the Affymetrix website that the probes in this set are:

				ATCTGTGCAHAGTTAACATTAGATC	Antisense
31377_r_at	14	397	115	GGTAAAAGCAGCCCAAGAAAAACAG	Antisense
31377_r_at	151	415	117	TAAAAGCAGCCCAAGAAAAACAGAC	Antisense
31377_r_at	544	199	119	AAAGCAGCCCAAGAAAAACAGACCA	Antisense
31377_r_at	40	17	122	CCAGCCCAAGAAAAACAGACCAACA	Antisense
31377_r_at	39	17	124	AGCCCAAGAAAAACAGACCAACAGA	Antisense
31377_r_at	41	17	125	GCCCAAGAAAAACAGACCAACAGAA	Antisense
31377_r_at	160	235	128	CAAGAAAAACAGACCAACAGAAAAG	Antisense
31377_r_at	253	309	130	AGAAAAACAGACCAACAGAAAAGCA	Antisense
31377_r_at	31	125	137	CAGACCAACAGAAAAGCAATGAGAG	Antisense
31377_r_at	32	125	138	AGACCAACAGAAAAGCAATGAGAGA	Antisense
31377_r_at	104	487	15	TACTTAGTTGTGAGATCCATCCCCT	Antisense
31377_r_at	144	363	19	TAGTTGTGAGATCCATCCCCTGGGT	Antisense
31377_r_at	422	209	201	AACAGTAACCCAAGAAAACATCATG	Antisense
31377_r_at	69	109	25	TGAGATCCATCCCCTGGCTTCATTC	Antisense

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31377_r_at    493  263  29   ATCCATCCCCTGGCTTCAGTCCCTG   Antisense
31377_r_at     12  453  39
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It is understood that an applicant need not teach, and preferably omits that which is well known in the art. *Hybritech Inc. v. Monoclonal Antibodies, Inc.*, 802 F.2d 1367, 1384, 231 USPQ 81, 94 (Fed. Cir. 1986) (accord *Capon v. Eshar*, 418 F.3d 1349 (Fed. Cir. 2005)). Therefore, Applicants are not required to disclose the probes on the Affymetrix chip, since these probes can be purchased on the Affymetrix array and their sequences can be found in the public domain.

Even if the identify of these probes were removed from the Affymetrix website or if Affymetrix ceased to sell the HG-U95av2 microarray, a skilled artisan would be fully capable of designing their own primers and probes to W26469 based on the sequence information available in GENBANK®. GENBANK® discloses about 350 known nucleotides for W26469 (and a long string of unknown nucleotides designated "N"). Regardless of the presence of some unknown nucleotides in the 350 known nucleotide sequence – a skilled artisan would have no difficulty designing a primer, primer set, or probe from this sequence for use in, e.g., Northern blotting, microarray hybridization, PCR (e.g., regular PCR, nested PCR, anchored PCR, RT-PCR, etc.), and other hybridization techniques. First, the Office has shown only that small portions of W26469 can hybridize to various genomic sequences. Genomic hybridization can easily be avoided by using RNA sample preparations. Second, non-specific hybridization can be avoided by modifying the length of a probe (a longer sequence having less likelihood of hybridizing to a non-specific target), selecting a different probe sequence (e.g., choosing primers with higher G-C content), employing a higher annealing and/or extension temperature, using different primer extension times, increasing the concentration of salt in a reaction buffer, varying the presence or amount of a denaturant, etc. These are all well-known, established, and accepted methods to routinely optimize and empirically identify the best hybridization conditions for a particular target sequence and selected primer/probe. *See, e.g.*, Davis et al. (1996) Basic Methods in Molecular Biology, 2nd Edition, page 116-117 (courtesy copy submitted herewith). Numerous papers teach parameters to consider for PCR primer design (e.g., Dieffenbach et al. (1993) Genome Res. 3:S30-S37) (courtesy copy submitted herewith) and algorithms one might employ to create efficient primers (e.g., Kampke et al. (2001) Bioinformatics 17:214-225) (courtesy copy submitted herewith). Indeed, a brief search of the internet identifies numerous primer design software programs, many of which were available

well before Applicants' priority date (e.g., "Primer3" [Steve Rozen and Helen J. Skaletsky (2000) "Primer3 on the WWW for general users and for biologist programmers. In: Krawetz S, Misener S (eds) Bioinformatics Methods and Protocols: Methods in Molecular Biology. Humana Press, Totowa, NJ, pp 365-386]). PCR and other hybridization techniques have been used for decades to detect RNA -- and the routine optimization required to strike upon an ideal hybridization probe/primer and condition is not undue, nor is it even burdensome. It is a standard molecular biology concern that is successfully addressed in thousands of molecular biology laboratories every day. Finally, even if one were not able to use a traditional 20-25 base pair primer designed from the GENEBANK® sequence given to measure the level of W26469 – one could surely employ the entire known portion of the W26469 sequence (about 350 nucleotides) to obtain high specificity in various hybridization techniques.

As such, no undue experimentation is required to detect the level of expression of SEQ ID NO:36. For at least these reasons, Applicants respectfully submit that the claims are enabled.

Written Description Rejection

The Office's written description rejection also finds basis on the use of SEQ ID NO:36 in the pending claims. For the following reasons, that rejection is respectfully traversed.

The Office is concerned that the structure of SEQ ID NO:36 is not sufficient to allow one to envision the structure of a reagent useful to assay the level of SEQ ID NO:36 in order to perform the claimed methods. To satisfy the written description requirement, Applicants need only "reasonably convey" sufficient characteristics so that a skilled artisan can "visualize or recognize the identity" of the invention. *Ralston Purina Co. v. Far-Mar-Co., Inc.*, 772 F.2d 1570, 1575 (Fed. Cir. 1985); *Regents of the University of California v. Eli Lilly, Co.*, 119 F.3d 1559, 1568 (Fed. Cir. 1997). As described above in the enablement section, in order to detect the level of expression of the nucleotide sequences recited in the pending claims, including SEQ ID NO:36, a skilled artisan need only look to GENBANK® (and the sequence listing provided for the instant application) to recognize that Applicants possessed the currently claimed methods.[1]

[1] To satisfy the written description requirement, Applicants need only provide enough detail such that, when that detail is coupled with the knowledge available to one of ordinary skill in the art, a skilled artisan would understand that at the time of filing the instant Application, Applicants possessed what they now claim. As discussed in the enablement section, GenieBank and SEQ ID NO:36 provide sufficient information to allow a skilled artisan to perform various hybridization techniques useful to detect the level

More specifically, there is adequate evidence that the nucleotide sequence available for SEQ ID NO:36 is sufficient to allow a skilled artisan to design probes and primers useful in various hybridization techniques and PCR methods to measure the level of SEQ ID NO:36 in a sample from a patient. Indeed, Applicants did use microarray technology with W26469 probes to assay the level of W26469 in samples. Accordingly, the specification reasonably conveys that Applicants possessed the claimed methods, and a skilled artisan would recognize the same. For at least these reasons, Applicants respectfully submit that the claims are adequately described.

CONCLUSION

In light of the above amendments, observations and remarks, Applicants respectfully submit that the presently claimed invention satisfies 35 U.S.C. §112, and is neither disclosed nor suggested by any art of record. Accordingly, reconsideration and allowance of all claims in this application is earnestly solicited.

Applicants' undersigned attorney may be reached in our New Jersey office by telephone at (862) 778-9308. All correspondence should continue to be directed to our below-listed address.

Respectfully submitted,

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of SEQ ID NO:36. As such, a skilled artisan would understand that Applicants possessed information sufficient to detect levels of SEQ ID NO:36. In fact, as disclosed in the specification, Applicants did exactly that using microarray technology.